

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 30, 2009 has been entered. Claims 1, 16-18, 31 and 32 have been amended. Claims 1-26, 31 and 32 are pending and currently under examination.

### ***Rejections Withdrawn***

2. In view of Applicant's amendments and arguments, the rejection of claims 1, 15-18, 31 and 32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

### ***Rejections Maintained***

#### ***Claim Rejections - 35 USC § 102/103***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The rejection of claims 1-26, 31 and 32 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Stephan et al. (U.S. Patent 4, 734,279) as evidenced by Rudd et al. (Science, 2001; 291: 2370-2376) and Shu et al. (Nahrung, 1998; 42(2): 68-70) is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) In Example 1 and 2 of the present application it is disclosed that bacterial exposure of the antimicrobial composition of the present invention results in 100% killing of the gram negative as well as gram positive bacteria; this further adds to the argument that synthetically glycosylated immunoglobulins of the present invention are both different from and has improved properties over the immunoglobulin's of Stephan et al.

2) Stephan et al. disclose in column 4, lines 5-15 that the immunoglobulins are able to capture fragments of the bacteria as a result of a preceding lysis of the bacteria by lysozyme, which are hereby supplied to the elimination process by immune cells; and that the immunoglobulins are able to capture only fragments of the bacteria does not imply that the immunoglobulins bind to bacterial surface antigens.

3) The present invention is directed towards intact pathogenic bacteria and the synthetically glycosylated immunoglobulins are directly involved in the lysis process of the gram negative bacteria.

Applicant's arguments have been considered and are deemed non-persuasive.

The rejected claims are drawn to an antimicrobial composition comprising lysozyme and synthetically glycosylated immunoglobulins directed towards antigens on the surface of Gram negative bacteria, wherein said synthetically glycosylated immunoglobulins have been produced by dissolving non-synthetically glycosylated immunoglobulins in a solution comprising disaccharide or monosaccharide under conditions resulting in synthetic glycosylation of said parental immunoglobulins, and wherein said antimicrobial composition has increased bactericidal activity at least in part as a result of said synthetic glycosylation.

With regard to Points 1 and 4, Applicant's assertions comprise only attorney's argument; said argument cannot be considered evidence unless it is an admission, in which case, it must be supported by an appropriate affidavit or declaration MPEP 2145.

Applicant is reminded that with regard to Applicant's assertion of unexpected results,

Applicant has failed to provide evidence supporting said assertion. The MPEP states:

716.02(b) Burden on Applicant

**BURDEN ON APPLICANT TO ESTABLISH RESULTS ARE UNEXPECTED AND SIGNIFICANT**

The evidence relied up should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) (Mere conclusions in appellants' brief that the claimed polymer had an unexpectedly increased impact strength "are not entitled to the weight of conclusions accompanying the evidence, either in the specification or in a declaration."); Ex parte C, 27 USPQ2d 1492 (Bd. Pat. App. & Inter. 1992) (Applicant alleged unexpected results with regard to the claimed

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soybean plant, however there was no basis for judging the practical significance of data with regard to maturity date, flowering date, flower color, or height of the plant.). See also *In re Nolan*, 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977) and *In re Eli Lilly*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) as discussed in MPEP § 716.02(c).

#### APPLICANTS HAVE BURDEN OF EXPLAINING PROFFERED DATA

"[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness." *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992).

#### DIRECT AND INDIRECT COMPARATIVE TESTS ARE PROBATIVE OF NONOBVIOUSNESS

Evidence of unexpected properties may be in the form of a direct or indirect comparison of the claimed invention with the closest prior art which is commensurate in scope with the claims. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) and MPEP § 716.02(d) - § 716.02(e). See *In re Blondel*, 499 F.2d 1311, 1317, 182 USPQ 294, 298 (CCPA 1974) and *In re Fouche*, 439 F.2d 1237, 1241-42, 169 USPQ 429, 433 (CCPA 1971) for examples of cases where indirect comparative testing was found sufficient to rebut a prima facie case of obviousness. The patentability of an intermediate may be established by unexpected properties of an end product "when one of ordinary skill in the art would reasonably ascribe to a claimed intermediate the contributing cause' for such an unexpectedly superior activity or property." *In re Magerlein*, 602 F.2d 366, 373, 202 USPQ 473, 479 (CCPA 1979). "In order to establish that the claimed intermediate is a contributing cause' of the unexpectedly superior activity or property of an end product, an applicant must identify the cause of the unexpectedly superior activity or property (compared to the prior art) in the end product and establish a nexus for that cause between the intermediate and the end product." *Id.* at 479.

#### Additionally, 716.01(c) Probative Value of Objective Evidence TO BE OF PROBATIVE VALUE, ANY OBJECTIVE EVIDENCE SHOULD BE SUPPORTED BY ACTUAL PROOF

Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence." "[A]ppellants have not presented any experimental data showing that prior heat-shrinkable articles split. Due to the absence of tests comparing appellant's heat shrinkable articles with those of the closest prior art, we conclude that appellant's assertions of unexpected results constitute mere argument."). See also *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); *Ex parte George*, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991).

#### ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

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The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

With regard to Point 2, while column 4, lines 5-15 recites "Lysozyme occurs, among other places, in saliva and chicken eggs. The enzyme cleaves in the bacterial cell wall between N-acetylmuraminic acid and N-acetylglucosamine. In this manner, the cell wall structure can be broken up (lysis). The fragments of the bacteria lysed in this manner can be captured by immunoglobulins and supplied to the elimination process by immune cells", the statement does not necessarily impart that the immunoglobulins are able to only capture fragments of the bacteria as implied by Applicant. The Examiner is of the position that said excerpt was used to clearly define the action lysozyme can have; as evidence by Applicant's disclosure at page 2, lines 26-31, where it discloses that it is well known in the art that gram positive bacteria are lysed in the presence of lysozyme whereas gram negative bacteria are not affected by lysozyme. Since it is taught that in the humoral immune system all of the immunoglobulins and most of the complement components are glycosylated; one of ordinary skill in the art would recognize that Stephen et al. comprises the same composition as that which has been claimed; they both comprise glycosylated immunoglobulins and lysozyme and therefore, would both be expected to function in the same manner.

With regard to Point 3, Stephan et al. disclose that the microorganisms (gram negative) are bound by the immunoglobulins in the presence of lysozyme, which implies that like the instant invention, Stephen et al. is geared towards intact pathogenic bacteria and the glycosylated immunoglobulins are directly involved in the lysis process of the Gram negative bacteria.

As previously presented, Stephan et al. disclose a composition comprising a lysozyme and an immunoenhancing amount of immunoglobulins IgG, IgM and IgA (see abstract; column 1, lines 10-20). Stephan et al. disclose that mice were infected with *Pseudomonas aeruginosa* and the animals were protected by the administration of the immunoglobulin preparation (see column 2, lines 35-44). Stephan et al. disclose that the composition can be incorporated into a vehicle, such as tablets or ointments. Moreover, Rudd et al. which disclose that in the humoral immune system all of the immunoglobulins and most of the complement components are glycosylated (see abstract).

Stephan et al. do not specifically disclose that the immunoglobulins have affinity to Gram positive bacteria, viruses or antigen determinants on the cell wall of Gram negative bacteria. Moreover, Stephan et al. do not specifically disclose that the lysozyme is conjugated to a monosaccharide.

Shu et al. disclose that polysaccharide chain attachment, which includes monosaccharides such as mannose, to lysozyme is critical for excellent emulsifying properties (see abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Stephan et al. with regard to immunoglobulins having affinity to Gram positive bacteria, viruses or antigen determinants on the cell wall of Gram negative bacteria because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Moreover, with regard to lysozyme conjugated to monosaccharide, "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art

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to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

With regard to claims 1, 16-18 and 22, it should be remembered that the products of the prior art reference appear to be the same as the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the process does not change properties of the product in an unexpected manner. See *In re Thorpe*, 227 USPTO 964 (CAFC 1985); *In re Marosi*, 218 USPTO 289, 29222-293 (CAFC 1983); *In re Brown*, 173 USPTO 685 (CCPA 1972). Even if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, great stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts to applicants product in order to overcome the aspect of the product's purity.

With regard to claim 2, claim limitations such as “for local use on mucosal membranes and/or skin” are being viewed as limitations of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 458.

With regard to claim 15, absent evidence to the contrary, the compositions of the prior art is identical to the composition as claimed, the glycosylated immunoglobulin

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necessarily has reduced complement fixation activity relative to said parental immunoglobulin.

With regard to claims 23-26, limitations such as the form of the composition and the range of the lysozyme and glycosylated immunoglobulins are being viewed as limitations of optimizing experimental parameters.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 recites the limitation "said parental immunoglobulins" in lines 8 and 9.

There is insufficient antecedent basis for this limitation in the claim.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 10, 12-18, 22-26 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Perraudin (EP 1 068 871 A1; Publication date: 1/17/01).

The rejected claims are drawn to an antimicrobial composition comprising lysozyme and synthetically glycosylated immunoglobulins directed towards antigens on the surface of Gram negative bacteria, wherein said synthetically glycosylated



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immunoglobulins have been produced by dissolving non-synthetically glycosylated immunoglobulins in a solution comprising disaccharide or monosaccharide under conditions resulting in synthetic glycosylation of said parental immunoglobulins, and wherein said antimicrobial composition has increased bactericidal activity at least in part as a result of said synthetic glycosylation.

Perraudin discloses medicaments comprising lysozyme and immunoglobulins (see paragraph 0035). Perraudin discloses that in the formulations, lysozyme can be provided from different sources including but not limited to egg white in an amount from 0.001g to 50 g per kg bodyweight per day or per 100 ml of liquid (see paragraph 0070). The immunoglobulins can be provided from sources including but not limited to bovine secretions, such as blood, colostrum and milk as well as human secretions such as blood, milk and other derivatives. Perraudin discloses that immunoglobulins can be produced from secretion liquids of immunized animals in an amount from 0.001g to 100g per kg bodyweight per day per 100 ml of liquid (see paragraph 0071). Since it is taught in the art that in the humoral immune system all of the immunoglobulins and most of the complement components are glycosylated; one of ordinary skill in the art would recognize that Perraudin comprises the same composition as that which has been claimed; they both comprise glycosylated immunoglobulins and lysozyme and therefore, would both be expected to function in the same manner.

With regard to claim 1, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the

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product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

With regard to claim 2, claim limitations such as "for local use on mucosal membranes and/or skin" are being viewed as limitations of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 458.

With regard to claim 15, absent evidence to the contrary, the compositions of the prior art is identical to the composition as claimed, the glycosylated immunoglobulin necessarily has reduced complement fixation activity relative to said parental immunoglobulin.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

***Conclusion***

6. No claim is allowed,

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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